

WHAT IS CLAIMED IS:

1. A method for enhancing or inducing immunity comprising administering to a patient a composition comprising a granzyme inhibitor.
2. The method of claim 1, wherein the composition comprising the granzyme inhibitor comprises an agent that can target the granzyme inhibitor to a cytotoxic T lymphocyte in the patient.
3. The method of claim 2, wherein the agent is an antibody.
4. The method of claim 1, wherein the granzyme inhibitor inhibits granzyme activity, inhibits granzyme transcription, inhibits granzyme translation, increases granzyme degradation, or destabilizes granzyme.
5. The method of claim 1, wherein the granzyme inhibitor inhibits granzyme activity.
6. The method of claim 1, wherein the granzyme inhibitor is a polypeptide, an anti-granzyme antibody, or a small molecule.
7. The method of claim 6, wherein the granzyme inhibitor is a polypeptide.
8. The method of claim 6, wherein the polypeptide is further defined as a fusion protein comprising a leader sequence.
9. The method of claim 7, wherein the polypeptide is a mimetic.
10. The method of claim 9, wherein the mimetic is a PI9 mimetic.
11. The method of claim 10, wherein the PI9 mimetic, comprises SEQ ID NO:16.

12. The method of claim 7, wherein the polypeptide is a serpin.
13. The method of claim 12, wherein the serpin is SPI6, PI9, PI-6, monocyte
5 neutrophil elastase inhibitor (MNEI), PI-8, or plasminogen activator inhibitor 2 (PAI-2).
14. The method of claim 12, wherein the serpin is SPI6.
15. The method of claim 12, wherein the serpin is PI9.
- 10 16. The method of claim 1, further defined as a method of enhancing or inducing immunity to a virus.
17. The method of claim 16, wherein the virus is HIV, LCMV, HCV, HTLV-1,
15 HTLV-2, EBV, HBV, human cytomegalovirus, Herpes simplex 1, Herpes simplex 2, hepatitis G, enterovirus, dengue fever virus, or rabies virus.
18. The method of claim 17, wherein the virus is HIV.
- 20 19. The method of claim 17, wherein the virus is LCMV.
20. The method of claim 1, further defined as a method of enhancing or inducing immunity to a cancer.
- 25 21. The method of claim 20, wherein the cancer is a cancer that escapes immune system recognition.
22. The method of claim 20, wherein the cancer is a melanoma, a colon cancer, a prostate cancer, a renal cancer, a non-Hodgkin lymphoma, a sarcoma, a B-cell leukemia,
30 a lung cancer, or a breast cancer.

23. The method of claim 1, wherein enhancing or inducing immunity comprises increasing the number of cytotoxic T-lymphocyte memory cells.

5 24. The method of claim 1, wherein enhancing or inducing immunity comprises augmenting cytotoxic T-lymphocyte function.

25. The method of claim 1, wherein enhancing or inducing immunity comprises augmenting cytotoxic T-lymphocyte memory cell development.

10 26. A method for enhancing or inducing immunity comprising expressing a granzyme inhibitor in the cytotoxic T-lymphocytes of a subject by introducing an expression construct comprising a DNA segment encoding the granzyme inhibitor under the control of a promoter active in the cytotoxic T-lymphocyte.

15 27. The method of claim 26, wherein enhancing or inducing immunity comprises increasing the number of cytotoxic T-lymphocyte memory cells.

28. The method of claim 26, wherein enhancing or inducing immunity comprises augmenting cytotoxic T-lymphocyte function.

20 29. The method of claim 26, wherein enhancing or inducing immunity comprises augmenting cytotoxic T-lymphocyte memory cell development.

25 30. A method for enhancing or inducing immunity comprising:
a) obtaining a cytotoxic T-lymphocyte that comprises an expression vector that comprises a DNA segment encoding a granzyme inhibitor under the control of a promoter active in the cytotoxic T-lymphocyte; and
b) administering the cytotoxic T-lymphocyte to a subject in need thereof.

30 31. The method of claim 30, wherein the expression vector is a viral expression construct.

32. The method of claim 31, wherein the viral expression construct is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, a herpesvirus, a polyoma virus, and a vaccinia virus.

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33. The method of claim 31, wherein the vector is a retroviral vector.

34. The method of claim 30, wherein the granzyme inhibitor inhibits granzyme activity, inhibits granzyme transcription, inhibits granzyme translation, increases granzyme degradation, or destabilizes granzyme.

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35. The method of claim 30, wherein the granzyme inhibitor inhibits granzyme function.

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36. The method of claim 30, wherein the granzyme inhibitor is a polypeptide or an anti-granzyme antibody.

37. The method of claim 36, wherein the polypeptide is a serpin.

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38. The method of claim 37, wherein the serpin is SPI6, PI9, PI-6, monocyte neutrophil elastase inhibitor (MNEI), PI-8, plasminogen activator inhibitor 2 (PAI-2).

39. The method of claim 37, wherein the serpin is SPI6.

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40. The method of claim 37, wherein the serpin is PI9

41. The method of claim 30, further defined as a method of inducing or enhancing immunity to a virus.

42. The method of claim 41, wherein the virus is HIV, LCMV, HCV, HTLV-1, HTLV-2, EBV, HBV, human cytomegalovirus, Herpes simplex 1, Herpes simplex 2, hepatitis G, enterovirus, dengue fever virus, or rabies virus.

5 43. The method of claim 42, wherein the virus is HIV.

44. The method of claim 42, wherein the virus is LCMV.

10 45. The method of claim 30, further defined as a method of enhancing or inducing immunity to a cancer.

46. The method of claim 45, wherein the cancer is a cancer that escapes immune system recognition.

15 47. The method of claim 45, wherein the cancer is a melanoma, a colon cancer, a prostate cancer, a renal cancer, a non-Hodgkin lymphoma, a sarcoma, a B-cell leukemia, a lung cancer, or a breast cancer.

20 48. The method of claim 30, wherein inducing or enhancing immunity comprises increasing the number of cytotoxic T-lymphocyte memory cells.

49. The method of claim 30, wherein inducing or enhancing immunity comprises augmenting cytotoxic T-lymphocyte function.

25 50. The method of claim 30, wherein inducing or enhancing immunity comprises augmenting cytotoxic T-lymphocyte memory cell development.

30 51. A method for inducing or enhancing immunity comprising:
a) obtaining a cytotoxic T-lymphocyte;
b) exposing the cytotoxic T-lymphocyte to a leader sequence-granzyme B inhibitor fusion protein; and

- c) administering the cytotoxic T-lymphocyte to a subject in need thereof.

52. The method of claim 51, wherein the cytotoxic T-lymphocyte is exposed to the leader sequence-granzyme B inhibitor fusion protein at a concentration of about 10nM to 1000nM tissue culture media.

53. The method of claim 52, wherein the cytotoxic T-lymphocyte is exposed to the leader sequence-granzyme B inhibitor fusion protein at a concentration of about 100nM in tissue culture media.

54. The method of claim 51, further defined as a method of inducing or enhancing immunity to a virus.

55. The method of claim 54, wherein the virus is HIV, LCMV, HCV, HTLV-1, HTLV-2, EBV, HBV, human cytomegalovirus, Herpes simplex 1, Herpes simplex 2, hepatitis G, enterovirus, dengue fever virus, or rabies virus.

56. The method of claim 55, wherein the virus is HIV.

57. The method of claim 55, wherein the virus is LCMV.

58. The method of claim 51, further defined as a method of enhancing or inducing immunity to a cancer.

59. The method of claim 58, wherein the cancer is a cancer that escapes immune system recognition.

60. The method of claim 58, wherein the cancer is a melanoma, a colon cancer, a prostate cancer, a renal cancer, a non-Hodgkin lymphoma, a sarcoma, a B-cell leukemia, a lung cancer, or a breast cancer.